PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61N 5/06 | A1

(11) International Publication Number: WO 00/64537

(43) International Publication Date: 2 November 2000 (02.11.00)

(21) International Application Number: PCT/US00/11248

(22) International Filing Date: 27 April 2000 (27.04.00)

(30) Priority Data:
60/131,313 27 April 1999 (27.04.99) US

(71) Applicant: THE GENERAL HOSPITAL CORPORATION doing business as MASSACHUSETTS GENERAL HOSPITAL [US/US]; 55 Fruit Street, Boston, MA 02114 (US).

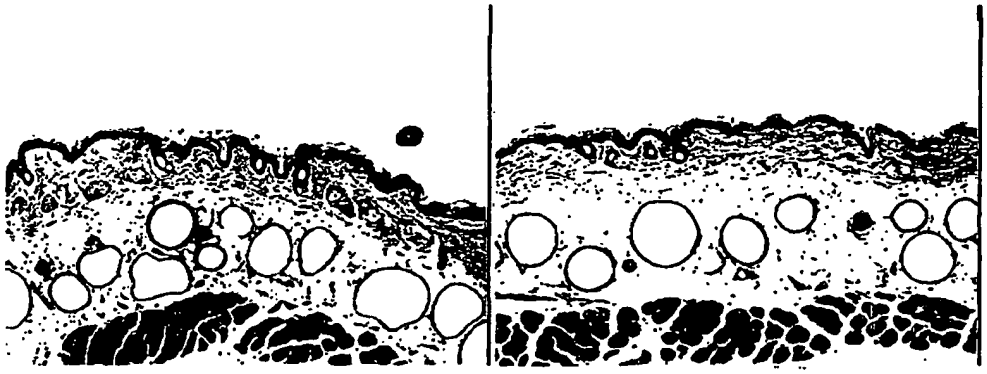
(72) Inventors: KOLLIAS, Nikiforos; 406 Sunset Road, Skillman, NJ 08558 (US). GILLIES, Robert; 388 Ocean Avenue, Apt. 1212, Revere, MA 02151 (US). TIAN, Wei, Dong; 10 Alhambra Road, West Roxbury, MA 02132 (US).

(74) Agents: ROTHENBERGER, Scott, D. et al.; Nutter, McClennen & Fish, LLP, One International Place, Boston, MA 02110-2699 (US).

(81) Designated States: CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: PHOTOTHERAPY METHOD FOR TREATMENT OF ACNE



(57) Abstract

The present invention is directed to methods for treating acne. The methods include exposing the subject afflicted with acne to ultraviolet light having a wavelength between about 320 to about 350 nm, such that the acne is treated e.g., inhibited, diminished, eradicated or prevented. In a preferred embodiment, the wavelength is 335 nm and is emitted by either a nitrogen laser or a third harmonic of a NdYAG laser. Treatments can be administered over a several week period, where the subject is exposed to sequential doses of ultraviolet light to obtain beneficial effects e.g., a reduction or elimination of the acne, e.g., an eradication or diminishment of the bacteria responsible for acne, e.g., *Propionibacterium acnes*.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

PHOTOTHERAPY METHOD FOR TREATMENT OF ACNE

BACKGROUND OF THE INVENTION

Acne is one of the most frequently presented dermatologic conditions. To date there is no single widely accepted treatment modality although a number of approaches exist. These approaches include topical or systemic antibiotics, benzoyl peroxide gels, oral 13-cis-retinoic acid, or hormones. Acne lesions (comedones) are the result of a complex interaction between hormones (androgens) and bacteria (*Propionibacterium acnes*) in the pilosebaceous unit. Acne results when the opening of the sebaceous glands is occluded, resulting in accumulation of sebum and fatty acids produced by the bacteria through lipase breakdown of lipids. The increase in sebum results in enlargement of the glands which in turn leads to inflammation and eventually to rupture of the glandular envelop. Release of the gland contents into the dermis produces changes in the structural matrix and may result in scarring. While acne is not a life threatening condition, it frequently produces discomfort, and can be disfiguring to a subject due to scarring.

Exposure of the skin to ultraviolet radiation has been reported to result in enlargement of the sebaceous glands. This has been found in photoaging studies in hairless mice. It is also known that sun exposure results in amelioration of acne. The response to sunlight may be either due to photodynamic activity (PDT) of coproporhyrin produced by the bacteria, *Propionibacterium acnes,* or due to an effect of the sunlight to the cell differentiation and proliferation. The PDT effect would lead to destruction of the bacteria which in turn would lead to improvement of acne. In this case, short wavelength visible radiation (405-410 nm) should be equally effective in improving acne. However, there is substantial evidence that both light and antibiotics reduce the fluorescence produced by coproporphyrin, the loss of which is not always related to amelioration of the acne condition.

SUMMARY OF THE INVENTION

The present invention is directed to methods for treating acne. The methods include exposing the subject afflicted with acne to ultraviolet light having a wavelength between about 320 to about 350 nm, such that the acne is treated, e.g., inhibited, diminished, eradicated or prevented. In a preferred embodiment, the wavelength is 335 nm and is emitted by a nitrogen laser, a third harmonic of a NdYAG laser, a tunable

OPO laser (Optical Parametric Oscillator), or a properly filtered mercury lamp or continuous wave lamp. Treatments can be administered over a several week period, where the subject is exposed to sequential doses of ultraviolet light to obtain beneficial effects, e.g., a reduction or elimination of the acne, e.g., eradication or diminishment of the bacteria responsible for acne, e.g., *Propionibacterium acnes*.

The present invention is also directed to methods for preventing acne. The methods include exposing the subject afflicted with acne to ultraviolet light having a wavelength between about 320 nm to about 350 nm, such that acne is prevented. In one embodiment, ultraviolet wavelengths useful in the invention are between about 325 nm to about 345 nm, preferably between about 330 to about 340 nm, more preferably between about 332 and about 337 nm, and most preferred at 335 nm.

The present invention is also directed to methods for reducing the amount or size of sebaceous glands in a subject. The methods include exposing the subject to ultraviolet light having a wavelength between about 320 and 350 nm, such that the amount or size of sebaceous glands in the subject are reduced.

The present invention is further directed to methods for treating disease states or conditions which cause or are associated with the generation of excess of sebum in sebaceous glands. The invention is also directed to methods for treating disease states or conditions which cause or are associated with the occlusion of sebaceous glands with accumulation of sebum and fatty acids produced by bacteria through lipase breakdown of lipids. These methods include exposing the subject to ultraviolet light having a wavelength between about 320 and 350 nm, such that the buildup of sebum and/or lipids in the sebaceous glands of the pilosebaceous units of the subject are reduced.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be more fully understood from the following detailed description taken in conjunction with the accompanying drawings, in which:

Fig. 1 is a histological section of hairless mouse skin exposed to 335 nm narrow band radiation. Note the absence of sebaceous glands in the exposed site (right), as opposed to the unexposed site (left).

Fig. 2. includes images of the superficial dermis of hairless mouse skin obtained *in vivo* with an infrared (1.06 μm) Laser Scanning Confocal Microscope.

Four control images corresponding to adjacent skin sites of unexposed hairless mouse skin at a depth of approximately 100 μm, with the sebaceous glands appearing at this depth as large ellipsoidal bodies (left panel), and four adjacent skin sites that received nine (9) exposures of 335 nm narrow band radiation at 7 J/cm^2 per exposure which corresponds to 0.25 of a minimum erythema dose (MED) at this wavelength (right panel). (Unstained sections, 30 x magnification, 0.9 NA in water, 250 x 250 μ field of view).

Fig. 3 is an action spectrum for changes in the native fluorescence of skin excited at 335 nm. This fluorescence has been found to be associated with pepsin digestible collagen cross links. The results presented are from hairless mouse skin (n=8) and each animal was exposed (single exposure) on different skin sites on its back at 7 J/cm^2 for each wavelength. Illumination was provided by a tunable OPO laser (Optical Parametric Oscillator).

DETAILED DESCRIPTION OF THE INVENTION

The features and other details of the invention will now be more particularly described and pointed out in the claims. It will be understood that the particular embodiments of the invention are shown by way of illustration and not as limitations of the invention. The principle features of this invention can be employed in various embodiments without departing from the scope of the invention.

In one aspect, the present invention is directed to methods for treating acne. The methods include exposing the subject afflicted with acne to ultraviolet light having a wavelength between about 320 to about 350 nm, such that the acne is treated, e.g., inhibited, diminished, eradicated or prevented. In a preferred embodiment, the wavelength is 335 nm and is emitted by a nitrogen laser, a third harmonic of a NdYAG laser, a tunable OPO laser (Optical Parametric Oscillator), or a properly filtered mercury lamp or continuous wave lamp. Treatments can be administered over a several week period, where the subject is exposed to sequential doses of ultraviolet light to obtain beneficial effects, e.g., a reduction or elimination of the acne, e.g., eradication or diminishment of the bacteria responsible for acne, e.g., *Propionibacterium acnes*.

The terms "treating" or "treatment" are intended to include eradication of, inhibition of, prevention of and/or diminishment of disease states or conditions

associated with pore blockage by sebum or lipids produced by the sebaceous glands. In a preferred embodiment, the occurrence of acne, measured by reduction of blackheads, whiteheads and/or the amount of sebaceous glands or size of sebaceous glands in a subject, is diminished, preferably by at least 30%, more preferably by at least 50%, even more preferably by at least 90%, and most preferably by at least 99%. Preferably, the occurrence of acne or a related condition is eliminated from the subject.

The term "subject" is intended to include living organisms susceptible to conditions or diseases caused or contributed to by overstimulation or production of sebum from sebaceous glands. Examples of subjects include humans, dogs, cats, cows, goats, and mice. The term subject is further intended to include transgenic species.

The term "acne" is art recognized and is intended to include acne vulgaris and acne rosacea. The term encompasses the condition(s) associated with the complex interactions between hormones and bacteria in the pilosebaceous unit which often result in comedones. Acne vulgaris is the most common skin disease seen in dermatologic practice which affects millions of people in the United States. Abnormal keratin production with obstruction of the follicular opening, increased production of sebum (lipids secreted by the androgen-sensitive sebaceous glands), proliferation of *Propionibacterium acnes* (anerobic follicular diphtheroids), follicular rupture and follicular mites (demodex) are commonly associated with acne.

In acne vulgaris, rupture of a follicle is the event which stimulates inflammation to form a "pimple," including accumulation of pus to form a "whitehead." "Blackheads" (an open comedo) consist of a plugged sebaceous follicle which contains melanin or melanin-oxidized substances which absorb light.

There is no doubt that acne is related to the presence of hyperactive sebaceous glands, no matter what the cause. Therefore, a method which results in diminution of sebaceous gland activity, might be a first necessary step in the development of successful treatment for acne. The present invention is directed to diminishing sebaceous gland activity and/or reduction or destruction of the sebaceous gland.

In another aspect, the present invention is also directed to methods for preventing acne. The methods include exposing the subject afflicted with acne to ultraviolet light having a wavelength between about 320 nm to about 350 nm, such that

acne is prevented. Therefore, the methods of the invention can be used prophylactically to reduce or eliminate the possibility of having follicle openings plugged with sebum, dirt and/or lipids.

In one embodiment, ultraviolet wavelengths useful in the invention are between about 320 nm to about 360 nm, between about 325 nm to about 345 nm, preferably between about 330 to about 340 nm, more preferably between about 332 and about 337 nm, and most preferred at 335 nm.

In yet another aspect, the present invention is also directed to methods for reducing the amount or size of sebaceous glands in a subject. The methods include exposing the subject to ultraviolet light having a wavelength between about 320 and 350 nm, such that the amount or size of sebaceous glands in the subject are reduced. The reduction of sebaceous glands in either size or number can be transitory, lasting several days to several weeks, or, more preferably, can be permanent.

The term "sebaceous gland" is art recognized and is a component of the pilosebaceous unit. Sebaceous glands are located throughout the body, especially on the face and upper trunk, and produce sebum, a lipid-rich secretion that coats the hair and the epidermal surface. Sebaceous glands are involved in the pathogenesis of several diseases, the most frequent one being acne vulgaris. Acne is a multi factorial disease characterized by the occlusion of follicles by plugs made out of abnormally shed keratinocytes of the infundibulum (upper portion of the hair follicle) in the setting of excess sebum production by hyperactive sebaceous glands. An advantage of the present invention is that the treatment can permanently alter the sebaceous gland, e.g., eliminate or reduce the number or size or sebaceous glands, rendering the sebaceous gland no longer susceptible to pore pluggage without the side effects of topical or oral drugs.

In still another aspect, the present invention is further directed to methods for treating disease states or conditions which cause or are associated with the generation of excess of sebum in sebaceous glands. The invention is also directed to methods for treating disease states or conditions which cause or are associated with the occlusion of sebaceous glands with accumulation of sebum and fatty acids produced by bacteria through lipase breakdown of lipids. These methods include exposing the subject to

ultraviolet light having a wavelength between about 320 and 360 nm, such that the buildup of sebum and/or lipids in the sebaceous glands of the pilosebaceous units of the subject are reduced.

The phrase "disease state or condition" is intended to include those sebaceous gland disorders which can be treated by a narrow range of ultraviolet light, e.g., between about 320 and 360, between about 320 and about 350 nm, preferably between about 325 nm and about 345 nm, more preferably between about 330 nm and about 340 nm, even more preferably between about 332 nm and about 337 nm, and most preferably about 335 nm. Examples of disease states or conditions which can be treated by the methods of the invention include sebaceous gland hyperplasia, acne vulgaris and acne rosacea. Of particular importance is the treatment of acne by the methods of the invention.

Typically the treatment of the subject with ultraviolet light at the preferred wavelengths of the invention is conducted such that the ultraviolet light has a fluence of between about 1 J/cm^2 and about 5 J/cm^2, preferably about 5 J/cm^2. In one embodiment, the treatment is performed between about 0.1 and about 0.5 of the minimum erythema dosage level. Typical fluence rates, for lasers, are between about 5 and 25 millijoules/pulse, more preferably between about 7 and 20 millijoules/pulse, even more preferably between about 10 and 15 millijoules/pulse, and most preferably about 10 millijoules per pulse at about a 10 nanosecond duration, thereby producing approximately between about 2 and about 2 megawatts. Typical fluence rates in non-laser applications are between about 2 and 50 milliwatts/cm^2.

In general the methods of the invention are performed over a period of time, usually several weeks, where a treatment is undertaken on a daily, every second or third day, or weekly basis. Ideally, a subject would undergo treatments 3 to 4 times a week for 3 to 4 weeks, with a individual exposures of about 5 J/cm^2 of the preferred ultraviolet wavelengths of the invention.

One skilled in the art would be able to choose an energy source which would produce a narrow ultraviolet wavelength between about 320 and about 350 nm, between about 325 and about 345 nm, between about 330 and about 340 nm, between about 332 and about 337 nm and specifically 335 nm. Such energy sources include fluorescent

lamps with an internal fluorescent coating that emits only in these particular wavelengths, nitrogen lasers, the third harmonic of NdYAG lasers, or a dye laser whose output is scanned over the area of the skin which requires treatment. The device can be in the shape of a flat panel for chest or back exposure, or it can have the shape of a semicircle for exposing the face.

Sunlight is composed of a broad spectrum of energy wavelengths, including ultraviolet light referred to as UVA and UVB. Although it is generally believed that sunlight generally ameliorates acne, several studies have actually shown that sunlight can increase the occurrence of acne or aggravate the condition. Gfesser and Worret (*Int. J. Derm.* 35, 116 (1996)) studied the effects of sun light and seasonal changes on acne. They concluded that exposure to sun light may have beneficial psychological effects but did not find that sunlight, in general, eliminated acne and, in certain individuals, increased outbreaks of acne. Similarly, Mills et al. (*Brit. J. Derm.* 98, 145 (1978) found that treatment of individuals with ultraviolet light between 280 and 320 nm actually caused acne to worsen and increased the creation of comedones. Sigurdsson et al. (*Dermatology* 194, 256 (1997)) studied the effects of "full spectrum"light treatment on acne vulgaris above 360 nm and concluded that visible light was a moderately effective treatment for acne. Therefore, it was surprising to unexpectedly find that a narrow band of ultraviolet light would have beneficial effects on the treatment of skin disorders such as acne.

It has been unexpectedly discovered that certain wavelengths of ultraviolet light, e.g., between about 320 to about 350 nm, are capable of producing biological effects in a wavelength specific way. The changes are produced in a fashion similar to selective photothermolysis, i.e., there appears to be a target organelle or appendix within the skin for each wavelength. In particular, it was discovered that multiple exposures to 335 nm light result in significant decrease in the frequency of appearance of sebaceous glands, e.g., in the skin of hairless mice. These wavelength specific biological changes can vary depending on whether continuous light (cw) or a pulsed laser is used.

The present invention is directed to accomplishing these goals by manipulating radiation at the wavelengths where fluorophores present in skin absorb. Selection of the appropriate energy, e.g., ultraviolet wavelength, produces a biological response, in

addition to producing changes in the native fluorescence of the skin. In particular, exposure of hairless mice skin to multiple suberythemogenic doses of 335 nm (±10 nm) produces significant reduction in the frequency of appearance of sebaceous glands as well as subtle changes in the collagen matrix. The reduction of the sebaceous gland density has been confirmed with routine histology as well as *in vivo* by laser scanning confocal microscopy (Figs. 1 and 2).

Previous studies have shown that 335 nm radiation is effective in reducing the native fluorescence of hairless mouse skin as well as the fluorescence of human skin. The fluence necessary to produce a twofold decrease is of the order of 1 J/cm^2. Unexpectedly, it was discussed that treatment of skin with exposure to ultraviolet light between the range of about 320 nm to about 350 nm, preferably between about 325 nm to about 345 nm, most preferably at 335 nm, reduced sebaceous gland activity and rendered and/or destroyed the sebaceous unit. For example, assuming a typical solar UVA radiation fluence rate of 4 mW/cm^2 (summer, no direct sun exposure), there is approximately 1 J/cm^2 of solar UVA corresponding to a 5 minute exposure. Changes in fluorescence are produced in a wavelength specific way i.e., the changes produced at 335 nm are produced with 5 times smaller dose than those at 360 nm (Fig. 3).

The mechanism of action for the depletion of sebaceous glands is not well understood because there is not a well characterized absorber in the pilosebaceous unit that absorbs light in this wavelength range. It is considered that a reduction in the number or size of sebaceous units in the hairless mouse would correspond to a similar response in the case of human skin. One consideration is that human skin is thicker with sebaceous glands located further in, which means that they would receive a reduced fluence rate, assuming that the same chromophores are present in both species. However, results on hairless mice indicate the applicability to human skin and the treatment of acne.

Both a continuous wave source as well as an optical parametric oscillator (OPO laser) have been utilized to treat skin. The skin response to the two light sources using similar fluences and fluence rates were different. The laser source (with 10 ns pulses) produced a greater level of inflammatory infiltrate without a clinical erythema response.

It is considered that the laser is as effective in reducing the frequency of appearance of sebaceous glands at substantially reduced fluences.

The experiments presented below investigate the details of the interaction of 335 nm radiation on the sebaceous glands of the hairless mouse demonstrate a precise dose response for the laser versus the cw narrow band source, and show the effect of 335 nm radiation on human skin *in vivo*.

Experimental Methods

1. **Dose Dependent Animal Studies.** The dose dependence of the reduction in sebaceous glands was tested on 12 mice (rhino mouse model). Sites on the back of each animal were tattooed and then received daily exposures at 0.05, 0.1, 0.2, 0.4, 0.8 MED of 335 nm radiation. The animals were exposed on one side of their back to cw radiation and on the other side with short pulse laser radiation (10 ns). The animals were followed up daily by confocal microscopy *in vivo* and biopsies were taken at time points after changes in the number of sebaceous glands were documented by confocal microscopy. Exposures were continued for up to 4 weeks on the sites that experienced no adverse effects (erythema, edema, scaling). Biopsies were taken from selected sites at the end of one month of exposures and the rest of the animals were followed up weekly at first and biweekly thereafter for up to 2 months to determine the rate of recovery. Frozen sections were obtained from the biopsied sites for autofluorescence microscopy analysis.

2. **Dose Dependence Human Studies.** Skin sites (2.5 cm in diameter) of the upper back of 12 normal human volunteers with mild to moderate acne will be exposed to 0.1, 0.25 and 0.5 of an MED (minimum erythema dose) of 335 nm radiation, three times a week. The MED will be first determined for each volunteer. Confocal microscopy images will be obtained from control and exposed sites on a weekly basis. At the end of the treatment period 3 nm biopsies will be taken from treated and control sites. Histological staining will include H&E as well as colloidal iron for evaluating changes induced to the structural matrix. The

exposed sites will be followed up for up to 2 months to evaluate recovery of the sebaceous glands.

3. **Chromophore Identification.** Skin from hairless mice and from humans will be obtained for fluorescence microscopy. Frozen and fresh sections will be prepared and fluorescence spectroscopy will be performed on the frozen and the fresh sections to identify the regions of the dermis where the 335 nm fluorescence originates from. High power pulsed laser radiation at 335 nm will then be used to determine whether the tissue site that absorbs at 335 nm, in order to produce fluorescence is also altered by the laser pulse or whether there are other organelles that are susceptible as well.

One of ordinary skill in the art will appreciate further features and advantages of the invention based on the above-described embodiments. Accordingly, the invention is not to be limited by what has been particularly shown and described, except as indicated by the appended claims. All publications and references cited herein, including those in the background, are expressly incorporated herein by reference in their entirety.

What is claimed is:

1. A method for treating acne, comprising exposing a subject afflicted with acne to ultraviolet light having a wavelength between about 320 to about 360 nm, such that said acne is treated.

2. The method of claim 1, wherein said wavelength is between about 325 to about 345 nm.

3. The method of claim 1, wherein said wavelength is between about 330 to about 340 nm.

4. The method of claim 1, wherein said wavelength is between 332 and 337 nm.

5. The method of claim 1, wherein said wavelength is about 335 nm.

6. The method of claim 1, wherein said ultraviolet light is produced by a nitrogen laser.

7. The method of claim 1, wherein said ultraviolet light is produced by a third harmonic of a NdYAG laser.

8. A method of claim 1, wherein said ultraviolet light has a fluence of between about 1 J/cm^2 and about 5 J/cm^2.

9. The method of claim 1, wherein said treatment is performed at between about 0.1 to about 0.5 minimum erythema dose.

10. The method of claim 1, wherein said treatment is conducted over multiple exposure periods.

11. A method for preventing acne, comprising exposing a subject afflicted with acne to ultraviolet light having a wavelength between about 320 nm to about 360 nm, such that acne is prevented.

12. The method of claim 11, wherein said wavelength is between about 325 to about 345 nm.

13. The method of claim 11, wherein said wavelength is between about 330 to about 340 nm.

14. The method of claim 11, wherein said wavelength is between 332 and 337 nm.

15. The method of claim 11, wherein said wavelength is about 335 nm.

16. The method of claim 11, wherein said ultraviolet light is produced by a nitrogen laser.

17. The method of claim 11, wherein said ultraviolet light is produced by a third harmonic of a NdYAG laser.

18. A method of claim 11, wherein said ultraviolet light has a fluence of between about 1 J/cm^2 and about 5 J/cm^2.

19. The method of claim 21, wherein said treatment is performed at between about 0.1 to about 0.5 minimum erythema dose.

20. The method of claim 21, wherein said treatment is conducted over multiple exposure periods.

21. A method for reducing the amount or size of sebaceous glands in a subject, comprising exposing a subject to ultraviolet light having a wavelength between about 320 and 360 nm, such that the amount or size of sebaceous glands in said subject are reduced.

22. The method of claim 21, wherein said wavelength is between about 325 to about 345 nm.

23. The method of claim 21, wherein said wavelength is between about 330 to about 340 nm.

24. The method of claim 21, wherein said wavelength is between 332 and 337 nm.

25. The method of claim 21, wherein said wavelength is about 335 nm.

26. The method of claim 21, wherein said ultraviolet light is produced by a nitrogen laser.

27. The method of claim 21, wherein said ultraviolet light is produced by a third harmonic of a NdYAG laser.

28. A method of claim 21, wherein said ultraviolet light has a fluence of between about 1 J/cm^2 and about 5 J/cm^2.

29. The method of claim 21, wherein said treatment is performed at between about 0.1 to about 0.5 minimum erythema dose.

30. The method of claim 21, wherein said treatment is conducted over multiple exposure periods.

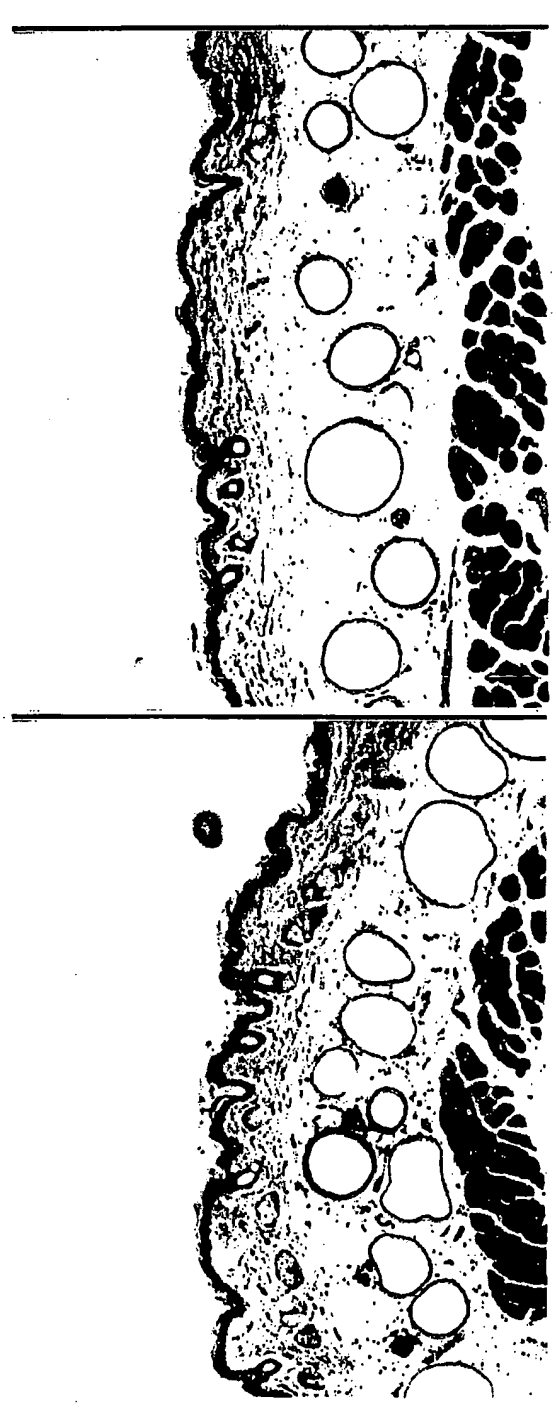


FIG. 1

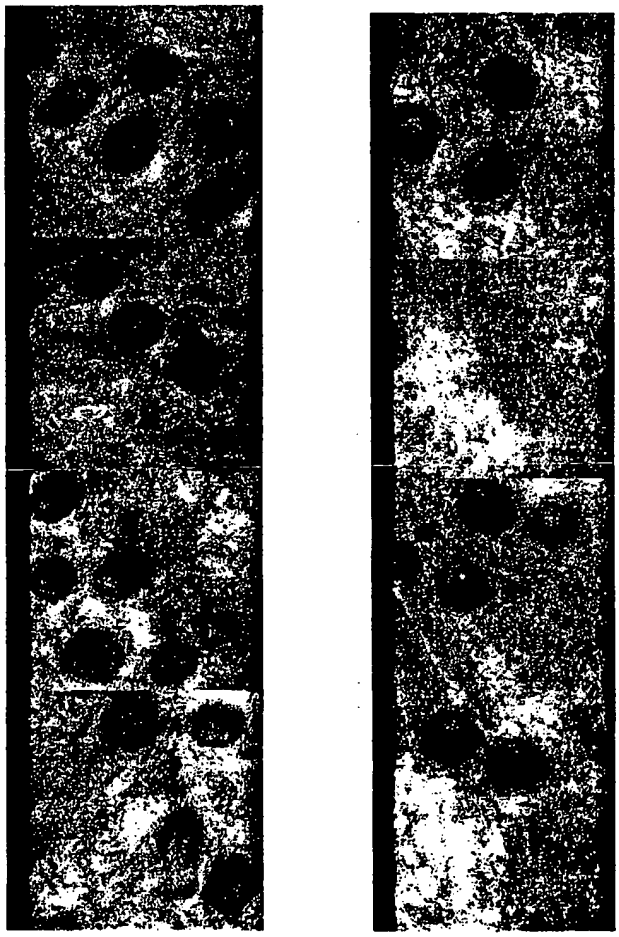


FIG. 2

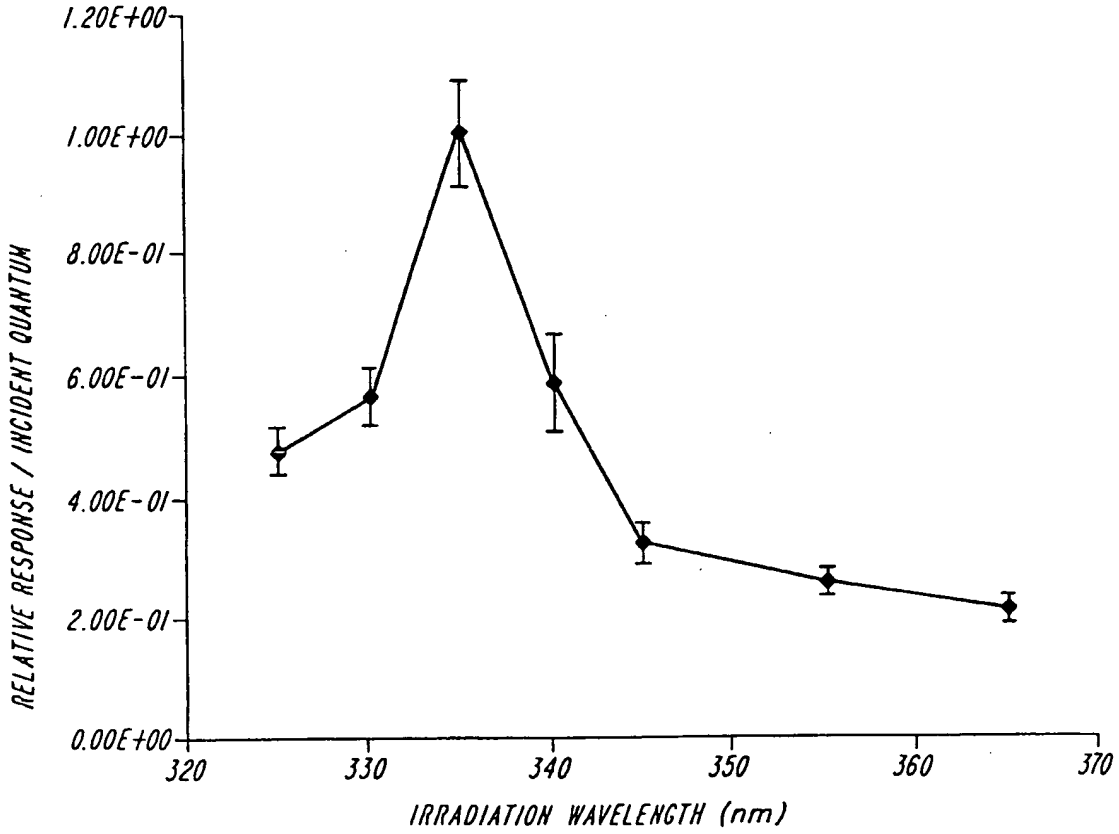

1.20E+00
1.00E+00
8.00E-01
6.00E-01
4.00E-01
2.00E-01
0.00E+00
RELATIVE RESPONSE / INCIDENT QUANTUM
320
330
340
350
360
370
IRRADIATION WAVELENGTH (nm)

FIG. 3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/11248

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 14899 A (OPTOMED OPTO MED SYS GMBH ;WILKENS JAN (DE)) 23 May 1996 (1996-05-23) page 12, line 19 - line 25	
A	US 4 287 554 A (WOLFF FRIEDRICH) 1 September 1981 (1981-09-01) column 1, line 27 - line 52	
A	EP 0 726 083 A (ESC MEDICAL SYSTEMS LTD) 14 August 1996 (1996-08-14) column 2, line 2 - line 12	
A	WO 98 33444 A (TRANSMEDICA INTERNATIONAL INC) 6 August 1998 (1998-08-06) page 36, line 11 - line 13	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 August 2000	07/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Petter, E

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/11248

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9614899 A	23-05-1996	DE 4440112 A	15-05-1996
		DE 19524461 A	30-01-1997
		AT 180177 T	15-06-1999
		CA 2205041 A	23-05-1996
		DE 59505982 D	24-06-1999
		EP 0790845 A	27-08-1997
US 4287554 A	01-09-1981	DE 2829117 A	07-02-1980
		DE 2846221 A	30-04-1980
		AT 358161 B	25-08-1980
		AT 608578 A	15-01-1980
		BE 870853 A	15-01-1979
		CA 1101495 A	19-05-1981
		CH 635000 A	15-03-1983
		DK 386678 A,B,	04-01-1980
		FI 782713 A,B,	04-01-1980
		FR 2430240 A	01-02-1980
		GB 2024393 A,B	09-01-1980
		IT 1160943 B	11-03-1987
		JP 1101784 C	25-06-1982
		JP 55008782 A	22-01-1980
		JP 56043431 B	12-10-1981
		LU 80242 A	07-03-1979
		NL 7809148 A	07-01-1980
		NO 782992 A,B,	04-01-1980
		SE 7809091 A	04-01-1980
EP 0726083 A	14-08-1996	US 5643334 A	01-07-1997
		AU 4440296 A	15-08-1996
		CA 2168636 A	08-08-1996
		FI 960539 A	08-08-1996
		JP 9000649 A	07-01-1997
WO 9833444 A	06-08-1998	AU 5917398 A	25-08-1998
		BR 9807816 A	08-03-2000
		CN 1251508 T	26-04-2000
		EP 1006902 A	14-06-2000
		US 6056738 A	02-05-2000